RESPONSE

A. Status of the Claims

Claims 38-60 were pending at the time of the Action, with claims 51-52 and 55-60 being withdrawn as directed to non-elected inventions. Claims 38-44 have been canceled without prejudice or disclaimer. Applicants reserve the right to pursue the subject matter of the canceled claims in one or more continuing applications. Claim 45 has been amended. Claim 61 has been added. No new matter was added by these amendments. Claims 45-61 are now pending with claims 51-52 and 55-60 being withdrawn as directed to non-elected inventions.

B. The Rejection Under 35 U.S.C. § 101

The Action rejects claims 38-44 under 35 U.S.C. § 101 as being directed to non-statutory subject matter. In particular, the Action states that the claims are directed to a product of nature. Applicants have amended the claims such that they are now directed to a pharmaceutical composition and specify that that the hyperimmune serum-reactive antigen is "isolated." Support for this amendment may be found in the specification at, for example, page 24, 7th paragraph (as numbered in WO 2004/099242). Applicants, therefore, respectfully request the withdrawal of this rejection.

C. The Claims Are Supported by Adequate Written Description in the Specification

Claims 38-50, 53, and 54 stand rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter that was not adequately described in the specification. Specifically, the Action asserts that the genus of "fragments" is not adequately described. Applicants traverse this rejection.

Claim 45 is currently the only independent claim under examination. In regard to hyperimmune serum-reactive antigens, current claim 45 states: "an isolated hyperimmune serum-reactive antigen comprising an amino acid sequence of SEQ ID NO: 364 or an

immunogenic fragment of SEQ ID NO: 364 comprising one or more of amino acid sequences 414-420, 427-437, 455-475, 494-510, 386-458, or 458-624 of SEQ ID NO:364." Such a hyperimmune serum-reactive antigen is adequately described in the present specification.

First, the antigen having the amino acid sequence of SEQ ID NO: 364 was identified due to its ability to elicit an immune response in humans (*see e.g.,* Specification, Examples 1, 3, and 4). As described in the present specification, the method by which relevant antigens, such as SEQ ID NO: 364, are identified involves using sera from individuals with antibodies against *S. agalactiae* (Specification, p. 4, last paragraph, to page 5, third paragraph; and Example 1). By screening antigens against sera from such individuals, the method identifies those antigens with a proven capability to stimulate an immune response. It is further noted that the antigen having the amino acid sequence of SEQ ID NO: 364 was selected more than 100 times in the screening of bacterial surface display libraries, which is an indication of its highly immunogenic property (Specification, Example 3, p. 57, last paragraph).

As noted above, claim 45 also recites "an immunogenic fragment of SEQ ID NO: 364 comprising one or more of amino acid sequences 414-420, 427-437, 455-475, 494-510, 386-458, or 458-624 of SEQ ID NO:364." As shown in Table 1A on page 77, these specific sequences identify the locations of identified immunogenic regions and predicted immunogenic amino acids of SEQ ID NO:364.

In view of the above, one skilled in the art would reasonably conclude that the inventor had possession of an isolated hyperimmune serum-reactive antigen comprising an amino acid sequence of SEQ ID NO: 364 or an immunogenic fragment of SEQ ID NO: 364 comprising one or more of amino acid sequences 414-420, 427-437, 455-475, 494-510, 386-458, or 458-624 of SEQ ID NO:364, based on the description provided for in the specification. Applicants, therefore, request the withdrawal of this rejection.

D. The Claims Are Enabled

The Action rejects claims 38-50, 53, and 54 under 35 U.S.C. § 112, first paragraph, for lack of enablement. The Action acknowledges that the specification is enabling for an isolated hyperimmune serum reactive *S. agalactiae* antigen comprising the amino acid sequence SEQ ID NO:364 or a hyperimmune serum reactive antigenic fragment consisting of the fragments of SEQ ID NO:364 specifically recited in claim 40. The Action asserts, however, that the specification does not reasonably provide enablement for any fragment of SEQ ID NO:364 or for a hyperimmune serum reactive antigenic fragment comprising the fragments of SEQ ID NO:364 specifically recited in claim 40. Applicants traverse this rejection.

As mentioned above, current claim 45 recites: "an isolated hyperimmune serum-reactive antigen comprising an amino acid sequence of SEQ ID NO: 364 or an immunogenic fragment of SEQ ID NO: 364 comprising one or more of amino acid sequences 414-420, 427-437, 455-475, 494-510, 386-458, or 458-624 of SEQ ID NO:364." The present specification enables a person of ordinary skill in the art to make and use the hyperimmune serum-reactive antigens encompassed by the claims without undue experimentation.

The Action's assertion that the specification is enabling only for an isolated hyperimmune serum reactive *S. agalactiae* antigen comprising the amino acid sequence SEQ ID NO:364 or a hyperimmune serum reactive antigenic fragment ***consisting of*** the fragments of SEQ ID NO:364 specifically recited in claim 40 (*i.e.*, amino acids 8-36, 40-64, 71-79, 88-94, 102-109, 118-127, 138-148, 151-159, 163-174, 192-198, 200-206, 220-233, 268-273, 290-301, 304-309, 316-323, 331-349, 378-391, 414-420, 427-437, 455-475, 494-510, 541-547, 549-555, 616-640, 1-60, 55-139, 212-308, 386-458 and 458-624 of SEQ ID NO:364) is incorrect. First, if the Examiner's reasoning that the use of the term "comprising" as the transitional phrase requires Applicants to enable "unlimited and unknown amino acids" (Action, p. 11) that may be added to

the claimed hyperimmune serum reactive antigenic fragment were proper, the "comprising" claim language could not be used with any claim, because in the case of nearly any composition or method it would be possible to attach thereto some additional "unlimited and unknown" component or step that would not be described in an applicant's specification. Thus, by the Examiner's reasoning, any claim to a polypeptide "comprising" a particular amino acid sequence, wherein the amino acid sequence is fully disclosed in the specification, could never be claimed since it is possible that the amino acid sequence might at some later point in time be attached to an object that is not presently disclosed. This is clearly not the proper standard for evaluating a specification's compliance with the enablement requirement.

To be enabling within the meaning of 35 U.S.C. § 112, the application must contain a description sufficient to enable one skilled in the art to make and use the claimed invention without unduly extensive experimentation. Furthermore, it is well-established law that an applicant need not enable technology developed or invented after the filing date, as such a disclosure would be impossible. *Chiron Corp. v. Genentech, Inc.*, 363 F.3d 1247, 1254 (Fed. Cir. 2004).

The specification provides the complete structure of SEQ ID NO: 364, and the Action concedes that the specification provides guidance on how to make a hyperimmune serum-reactive antigen comprising SEQ ID NO: 364 (Action, p. 10). Based on the disclosure of SEQ ID NO: 364, a person of ordinary skill in the art can readily identify and make a hyperimmune serum-reactive antigen comprising one or more of amino acid sequences 414-420, 427-437, 455-475, 494-510, 386-458, or 458-624 of SEQ ID NO:364. As described in the specification, these particular amino acids of SEQ ID NO:364 are locations of identified immunogenic regions and predicted immunogenic amino acids of SEQ ID NO:364 (*see* Table 1A on page 77). Additionally, fragments of SEQ ID NO:364 were demonstrated to be highly reactive with

individual human sera (Specification, Example 4, and Table 2). Accordingly, it would be predicted that polypeptides comprising these immunogenic regions would be hyperimmune serum-reactive antigens. Furthermore, assessing whether an isolated hyperimmune serum-reactive antigen comprising an immunogenic fragment of SEQ ID NO: 364 comprising one or more of amino acid sequences 414-420, 427-437, 455-475, 494-510, 386-458, or 458-624 of SEQ ID NO:364 was capable of eliciting an immune response would not require undue experimentation because it could be accomplished by routine screening using methods such as those described in Example 4 in the present specification (*see In re Wands*, 858 F.2d 731, 737 (Fed. Cir. 1988).

Applicants also provide the declaration of Dr. Senn (the Senn Declaration) as further evidence of the enablement of the current claims. The Senn Declaration describes both active and passive immunizations studies using an isolated hyperimmune serum-reactive antigen encompassed by the current claims. Dr. Senn is the Head of Infectious Disease Models at Intercell AG, which is the assignee of the present application. The gbs2018 antigen used in these studies corresponds to amino acids 36 to 612 of SEQ ID NO: 364 (Senn Declaration, para. 3). Thus, this antigen is within the scope of the current claims. The gbs0031 antigen used in the study is a known protective protein antigen, and was used as a positive control (Senn Declaration, para. 4 and 7). This known protective antigen is also disclosed in the present specification (*see e.g.* paragraph bridging pages 60-61). Animals used in the study were pre-screened for pre-existing GBS-specific antibodies by testing their sera with ELISA and only animals without a significant reaction were used in the study (Senn Declaration, para. 4, 5, and 7).

In the passive immunization studies, CD-1 mice were immunized intraperitoneally with 150 µl of an isolated hyperimmune serum-reactive antigen encompassed by the current claims.

The rabbit hyperimmune sera was prepared as describe in paragraph 4 of the Senn Declaration. The gbs2018 or gbs0031 rabbit hyperimmune sera was administered to the mice 1 to 3 hours before the bacterial challenge (Senn Declaration, para. 5). As a negative control, mice were immunized with 150 µl of phosphate buffered saline (PBS) (Senn Declaration, para. 5).

The mice were challenged with *S. agalactiae* strains C388/90 (serotype Ia), A909 (serotype Ia), ATCC12401 (serotype Ib), ATCC12403 (serotype III), COH1 (serotype III), ATCCBAA22 (serotype III), 2603V/R (serotype V), ATCC49447 (serotype V), and ATCCBAA23 (serotype V) (Senn Declaration, para. 5). Protection was measured by a lethal sepsis model (Senn Declaration, para. 5). As shown in Figures 1A to 1D attached to the Senn Declaration, the gbs2018 hyperimmune serum-reactive antigen increased survival of the immunized mice as compared to the controls given PBS (Senn Declaration, para. 6). Moreover, the mice immunized with the gbs2018 hyperimmune serum-reactive antigen also showed increased survival when compared to the positive-control mice immunized with gbs0031 (Senn Declaration, para. 6). Thus, the passive immunization study demonstrated that a gbs2018 antigen corresponding to amino acids 36 to 612 of SEQ ID NO: 364 produces a protective immune response against challenge with *S. agalactiae* (Senn Declaration, para. 9).

For active immunization studies, CD-1 female mice were immunized by subcutaneous injection with 25 µg of the recombinant gbs2018 or gbs0031 antigens adjuvanted with Complete Freund adjuvant (CFA) or 1% ALUM (Senn Declaration, para. 7). Animals were boosted twice with the same amount of antigen and Incomplete Freund adjuvant (IFA) at days 14 and 28 (Senn Declaration, para. 7). Mice immunized with PBS and adjuvant served as negative controls (Senn Declaration, para. 7). Mice immunized with gbs0031 or *S. agalactiae* lysate from the strain with which the mice were subsequently challenged served as positive controls (Senn Declaration, para. 7). Protection was measured by a lethal sepsis model (Senn Declaration, para. 7).

As shown in Figures 2A and 2B in the Senn Declaration, protective immunity was achieved by active immunization with gbs2018. Figure 2A shows the results of challenge with 1 x 10^6 cfu of ATCC12401 (serotype Ib) (Senn Declaration, para. 8). Mice immunized with gbs2018 had approximately a 50% survival rate 10 days post challenge, whereas the negative control mice had a survival rate of about 30% 10 days post challenge (Senn Declaration, para. 8). Mice immunized with the positive control Sip or lysate had survival rates of about 65% and 90%, respectively, 10 days post challenge (Senn Declaration, para. 8). Figure 2B shows the results of challenge with 1 x 10^8 cfu of ATCC49447 (serotype V) (Senn Declaration, para. 8). Mice immunized with gbs2018 had approximately a 50% survival rate 11 days post challenge, which was better than the survival rates observed for mice immunized with the positive and negative control groups at the same time point (Senn Declaration, para. 8).

In view of the above, the present specification contains a description sufficient to enable one skilled in the art to make and use the claimed invention without unduly extensive experimentation. Applicants, therefore, respectfully request the withdrawal of the rejection.

E. The Claims Are Definite

Claim 39 stands rejected under 35 U.S.C. § 112, second paragraph, as being indefinite. The Action asserts that because tables 1A, 1B, 2, 4, 5, 6, and 7, which are referenced in claim 39, contain several sequences, there is no practical way of defining the invention clearly. This rejection is moot in view of the cancellation of claim 39.

F. The Objection to Claim 38 is Overcome

Claim 38 is objected to because it recites non-elected sequences. The current claims recite elected sequences only. Applicants, therefore, request the withdrawal of this rejection.

G. The Claims Are Novel Over Telford

The Action rejects claims 38-49 and 53-54 under 35 U.S.C. § 102(b) as being anticipated by Telford *et al.* Accession No. ABP28545 and WO 2002/34771. The Action provides an alignment of SEQ ID NO:364 of the presently claimed invention with ABP28545. Although the aligned sequences are not identical, the Action argues that Telford teaches a hyperimmune serum-reactive antigen comprising a fragment of SEQ ID NO:364. Applicants traverse this rejection.

Current claim 45 recites an isolated hyperimmune serum-reactive antigen comprising an amino acid sequence of SEQ ID NO: 364 or an immunogenic fragment of SEQ ID NO: 364 comprising one or more of amino acid sequences 414-420, 427-437, 455-475, 494-510, 386-458, or 458-624 of SEQ ID NO:364. Telford does not disclose SEQ ID NO:364 or the fragments of SEQ ID NO:364 recited in the current claim. Telford, therefore, does not anticipate the current claims. Applicants respectfully request the withdrawal of this rejection.

H. The Claims Are Novel Over Glaser

The Action rejects claims 38-49 and 53-54 under 35 U.S.C. § 102(b) as being anticipated by Glaser *et al.* Accession No. ADV88412 and FR 2824074. The Action provides an alignment of SEQ ID NO:364 of the present specification with SEQ ID NO:806 of Glaser indicating that the sequences are identical. The Action states that Glaser teaches that pharmaceutical compositions comprising its disclosed peptides are useful in the treatment of *S. agalactiae* infection. Applicants traverse.

Glaser does not anticipate the current claims because Glaser does not teach a pharmaceutical composition comprising an isolated hyperimmune serum-reactive antigen comprising an amino acid sequence of SEQ ID NO: 364 or an immunogenic fragment of SEQ ID NO: 364 comprising one or more of amino acid sequences 414-420, 427-437, 455-475, 494-510,

386-458, or 458-624 of SEQ ID NO:364. Glaser appears to describe an *S. agalactiae* sequencing project. The English abstract indicates that Glaser (FR2824074A1) discloses 2,344 sequences. While Glaser discloses thousands of sequences reportedly obtained from *S. agalactiae*, it does not appear to disclose a single example where even one of these sequences was shown to elicit an immune response in an animal. Glaser has done nothing more than venture a guess that one or more of the thousands of *S. agalactiae* genes that were sequenced and listed in the specification would be useful in a pharmaceutical composition. In order to obtain Applicants' claimed composition from Glaser, a person of ordinary skill in the art would have to analyze an enormous number of *S. agalactiae* sequences. This is analogous to a "needle-in-the-haystack" approach. Courts have found no anticipation from these types of disclosures. *See Ex parte Garvey*, 41 U.S.P.Q. 583 (Pat & Trademark Office Bd. App. 1939).

A claim cannot be anticipated by a reference if the allegedly anticipatory disclosure is not enabled. Mere naming or description of the subject matter is insufficient if it cannot be produced without undue experimentation. MPEP § 2121.01; *see also Elan Pharms, Inc. v. Mayo Found. for Med. Educ. & Research*, 304 F.3d 1221, 1228 (Fed. Cir. 2002) (stating "The anticipating reference 'must disclose every element of the challenged claim and enable one skilled in the art to make the anticipating subject matter.'"). Glaser's mere ventured guess that one or more of the thousands of *S. agalactiae* genes that were listed in the Glaser specification may be useful in a pharmaceutical composition is clearly not an enabling disclosure of the subject matter of the current claims.

In contrast to the lack of guidance in the Glaser disclosure as to which *S. agalactiae* sequences may be effective antigens, Applicants' specification identifies hyperimmune serum-reactive antigens with a proven ability to stimulate an immune response. As discussed above, the method by which relevant antigens, such as SEQ ID NO: 364, were identified involved using

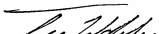
sera from individuals with antibodies against *S. agalactiae* (Specification, p. 4, last paragraph, to page 5, third paragraph; and Example 1). By screening antigens against sera from such individuals, the method identified antigens with a proven ability to stimulate an immune response.

In view of the above, the current claims are not anticipated by Glaser. Applicants, therefore, request the withdrawal of this rejection.

I. Conclusion

Applicants believe this paper to be a full and complete response to the Office Action dated December 13, 2006. Applicants respectfully request favorable consideration of this case in view of the above comments. Should the Examiner have any questions, comments, or suggestions relating to this case, the Examiner is invited to contact the undersigned Applicants' representative at (512) 536-5654.

Respectfully submitted,



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